REMARKS

Claims 1-11 are pending. Claim 4 is withdrawn. Claim 8 is amended. Claim 12 is added. Accordingly, upon entry of the amendment, claims 1-12 will be pending.

Claim 8 has been amended and claim 12 has been added to claim more fully the recited subject matter and to make minor editorial changes. Support for the amendment may at least be found in the originally filed specification, for example, at page 13, lines 1-6. No new matter is added.

Amendment of the claims herein is not to be construed as acquiescence to any objections/rejections set forth in the instant Office Action and were done solely to expedite prosecution of the application. Applicants reserve the right to pursue the subject matter of the claims as originally filed in this or one or more subsequent patent applications.

Claim Rejections – 35 U.S.C. §112

Claim 8 is rejected under 35 U.S.C 112, second paragraph, as allegedly indefinite. The Office Action at page 4 alleges that claim 8 is unclear for reciting "wherein said cell is substantially unable to divide." Applicants respectfully disagree and traverse the rejection.

Without acquiescing to the reasoning underlying the rejection and in order to expedite prosecution, Applicants have amended claim 8 to recite "wherein said cell divides at a rate that is less than about 50% of the rate of division of corresponding cells which are not treated to prevent cell division." Support for the amendment is at least found in the specification as filed, for example, at page 13, lines 1-6. Applicants respectfully submit that the metes and bounds of claim 8 are clear. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Claim Rejections – 35 U.S.C. §103

Claims 1-3 and 5-11 are rejected under 35 U.S.C §103(b) in view of U.S. 5,891,432 to Hoo et al. ("Hoo") and U.S. Patent Publication 2003/0091640 to Ramanathan et al. ("Ramanathan"). Applicants respectfully disagree and traverse the rejection.

In order to make out a *prima facie* showing of obviousness, the Examiner must establish that there is some motivation in one or the other of the cited references or in the state of the art at the time the invention was made to combine the references, the combination of references must teach or suggest each and every element of the claimed invention, and there must be some reasonable expectation of success in making and using the invention.

The presently claimed invention is a composition suitable for administration to a subject, said composition comprising a virus or a cell and a fusion polypeptide, said fusion polypeptide comprising a first amino acid sequence which comprises a cell-surface binding moiety and a second amino acid sequence comprising a ligand for a cell surface polypeptide of a leukocyte, wherein said composition includes said fusion polypeptide bound to said virus or said cell and includes said fusion polypeptide which is not bound to said virus or said cell, and wherein said fusion polypeptide is bound to a lipid on said virus or said cell by said cell—surface binding moiety.

Applicants have discovered that compositions comprising bound and free fusion polypeptide, where the bound fusion polypeptide is bound to a lipid on the cell by a cell—surface binding moiety are effective for modulating an immune response. This is at least shown in the specification at Example 6, in which two groups of cells were prepared and, after being incubated with a fusion protein of the invention that can bind a lipid on the cell surface, one group was washed and the other group was not. Example 6 describes the results of vaccinating mice with the washed and unwashed groups of cells that had been incubated with the fusion protein:

> Approximate percentages of mice surviving tumor-free to day 70 after challenge were: WT, 15%; soluble GM-CSF, 50%; GPI-GM-CSF washed, 60%; GPI-GM-CSF unwashed, 85%. Thus, even though the GPI-GM-CSF washed vaccine contained over a thousand-fold less GM-CSF than the unwashed soluble, administration of cells decorated with GPI-GM-CSF was more effective. **Furthermore, the GPI-GM-CSF unwashed vaccine, *in which some molecules were not attached to a cell*, was even more effective.**" [emphasis added; page 177, line – page 178, line 5]

Applicants were the first to appreciate that administering a composition of the invention containing both fusion protein bound to cells by a lipid (e.g., glycosylphosphatidylinositol) and unbound fusion protein (i.e., the unwashed cells described in Example 6) was effective in vaccinating mice against tumor development. Thus, the presently claimed invention is based, at least in part, on these discoveries.

In contrast, Hoo fails to teach or suggest such a fusion protein that is bound to a lipid of a cell. Instead, Hoo teaches that a fusion protein may be attached to a cell by a variety of transmembrane domains (col. 7, ln. 21 – col. 8, ln. 14) that are inserted into the plasma membrane. Thus, Hoo does not teach or suggest a composition containing a fusion polypeptide bound to a lipid on a virus or cell by a cell-surface binding moiety, as presently claimed.

As acknowledged by the Examiner on page 6 of the Office Action, "Hoo do not specifically state that a lipid is the target of their cell-surface binding moieties." The Examiner has further cited Ramanathan as an alleged remedy for the deficiencies of Hoo. However, the Examiner's reliance on Ramanthan is misplaced.

Applicants respectfully submit that there is no motivation to combine Ramanathan with Hoo in the manner proffered by the Examiner to arrive at Applicants' claimed composition. Hoo teaches a cellular vaccine having a membrane-bound fusion protein (Abstract). Ramanathan teaches delivery of a therapeutic or diagnostic agent which is covalently bound to a cell uptake promoter (e.g., a lipid). In the context of Ramanathan, "The cell uptake promoter enhances the intracellular access of the conjugate." [paragraph 0073]. This activity is in contrast to the fusion proteins of Hoo, which are membrane-bound.

As stated in *In re Gordon* and M.P.E.P. §2143.01: "If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). Because combining Hoo with Ramanathan would render the fusion proteins of Hoo unsatisfactory for their intended purpose, one would not be motivated to combine Hoo and Ramanathan.

Even so, Applicants respectfully submit that Hoo and Ramanathan either alone or in combination, do not teach or suggest "a composition suitable for administration to a subject, said composition comprising a virus or a cell and a fusion polypeptide, said fusion polypeptide comprising a first amino acid sequence which comprises a cell—surface binding moiety and a second amino acid sequence comprising a ligand for a cell surface polypeptide of a leukocyte, wherein said composition includes said fusion polypeptide bound to said virus or said cell and includes said fusion polypeptide which is not bound to said virus or said cell, and wherein said fusion polypeptide is bound to a lipid on said virus or said cell by said cell—surface binding moiety" as required by instant claim 1 and dependent claims thereof.

In particular, the Examiner has cited claims 1 and 12 of Hoo in support of the rejection. However, claims 1 and 12 of Hoo do not teach or suggest a fusion protein comprising a cell-surface binding moiety and a ligand for a cell surface polypeptide of a leukocyte (e.g., GPI-GM-CSF). At best, Hoo teaches a cell having a membrane bound fusion protein comprising Granulocyte Macrophage-Colony Stimulating Factor (GM-CSF) fused to a heterologous membrane attachment domain (Claim 1). Claim 1 of Hoo does not teach or suggest that the Granulocyte Macrophage-Colony Stimulating Factor (GM-CSF) fused to a heterologous membrane attachment domain is additionally present as unbound protein. Likewise, claim 12 also does not provide such a teaching or suggestion. Rather Claim 12 specifies that the disease-associated antigen or immunogenic epitope is fused to the membrane-bound fusion protein Hoo, but is silent regarding any unbound fusion protein comprising Granulocyte Macrophage-Colony Stimulating Factor (GM-CSF) fused to a heterologous membrane attachment domain.

Thus, the cited references do not teach or suggest the feature of **bound and unbound fusion protein** comprising a cell-surface binding moiety and a ligand for a cell surface polypeptide of a leukocyte, as recited in the claims

In sum, there is nothing in either of the cited references or in the state of the art at the time the invention was made that provides one of ordinary skill in the art with motivation to combine the references in the manner proffered by the Examiner. Assuming *arguendo* that there were such motivation, the combination does not teach or suggest each and every element of the claimed invention because neither reference teaches or suggests bound and unbound fusion protein as recited in the claims. Therefore, because the cited combination of references does not put one of ordinary skill in the art in possession of the claimed invention, one of ordinary skill in the art would not have a reasonable expectation of success in making and using the claimed invention.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Obviousness-type Double Patenting

The Office Action states that the instant claims are rejected under the judicially created doctrine of obviousness type double patenting in view of several co-pending applications. Upon notification of otherwise allowable subject matter in the instant case, Applicants will address the double patenting rejections.

CONCLUSION

In view of the foregoing amendments and arguments, Applicants respectfully request reconsideration and withdrawal of all pending objections/rejections and allowance of the applications with claims 1-3 and 5-12 presented herein. If a telephone call with Applicants' representative would be helpful in expediting prosecution of the application, Applicants invite the Examiner to contact the undersigned at the telephone number shown below.

Applicants submit this paper in response to the office action dated January 3, 2011, in the above-referenced patent application along with a petition for a two-month extension of time, and the required fees based on small entity status. Applicants believe that no additional fees are required for consideration and entry of this paper. Nevertheless, Applicants hereby authorize the Director to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to Deposit Account No. **04-1105**, under Order No. 85849DIV5(211111).

Dated: June 3, 2010

Respectfully submitted,

Electronic signature: /Elbert Chiang, Ph.D./
Elbert Chiang, Ph.D.
Registration No.: 60,325
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(617) 517-5502
Attorneys/Agents For Applicant